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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,941	08/09/2001	John R. Stuelpnagel	A-67616-4/RMS/DCF/SRN	6890

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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,941	STUELPNAGEL ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1 April 2004 has been entered.

Status of the Claims

2. This action is in response to papers filed 1 April 2004 in which claims 1 and 6 were amended and claims 11-12 were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 4 December 2003 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed and are discussed below as they apply to the instant grounds for rejection. New grounds for rejection, necessitated by amendment, are discussed.

Claims 1-5 and 6-12 are under prosecution.

Claim Rejections - 35 USC § 112

35 U.S.C. 112: first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 6-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation "when no bleed-through occurs" is added to the newly amended Claim 6 from which Claims 7-10 depend and new Claim 12. However, the specification fails to define or provide any disclosure to support such claim recitation. Applicant points to page 31, line 30 through page 33, line 30 for support for the above recitation. The cited passage describes bleed through signature as comprising over-lapping band width frequencies. However, the cited passage does not teach measuring a signal when no bleed-through occurs. And a review of the specification reveals no such teaching. Hence, the recitation introduces subject matter not described in the specification.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED.

APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE" (emphasis added).

35 U.S.C. 112: second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is indefinite for the recitation "the respective subpopulation of microspheres" because the recitation lacks proper antecedent basis in the claim.

Claim Rejections - 35 USC § 102/103

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application

designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claim 12 is rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lockhart et al (U.S. Patent No. 6,040,138, filed 15 September 1995).

Regarding Claim 12, Lockhart et al disclose a method comprising acquiring reference signals from subpopulations at discrete sites on an array by detecting signals in channels i.e. fixed excitation illumination (Column 23, lines 47-56) determining a threshold measure by comparing the reference signal to a threshold for each subpopulation (Column 23, line 57-Column 24, line 6) acquiring a first signal for each of a plurality of discrete sites and determining if the signal is within a threshold measure for the respective subpopulation (Column 23, line 42-Column 24, line 64) and wherein when the signal is within the threshold, the discrete site contains a positive signal (Column 24, lines 59-64).

The preceding rejection is based on judicial precedent following In re Fitzgerald, 205 USPQ 594 because Lockhart et al is silent with regard to bleed-through. However, the absence of bleed-through recited in Claim 12 is deemed to be inherent in the fixed excitation illumination and comparison of absolute intensities in Lockhart et al (Column 23, lines 42-56) because Lockhart et al desires exact illumination and detection and hence absence of bleed through. Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Lockhart and to measure signals when no bleed through occurs for the expected benefit of exact illumination and detection as they desire.

The burden is on applicant to show that the claimed (property X) is either different or non-obvious over that of [1st ref.]

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (U.S. Patent No. 6,327,410 B1, filed 11 September 1998) in view of Gingeras (U.S. Patent No. 6,228,575, filed 7 February 1997).

Regarding Claim 1, Walt et al disclose a method of determining the presence of a target analyte in a sample comprising acquiring a first data image (i.e. optical signature) of a random array composition comprising a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation each comprising a bioactive agent wherein said microspheres are distributed on said surface such that each of said discrete sites contain no more than one microsphere (Column 3, lines 35-45; Column 5, line 61-Column 6, line 29; and Fig. 5 & 7) mapping a grid (i.e. matrices) onto said first data image to create a registered first data image (i.e. optical signature) contacting said random array with a sample, acquiring a second data image from said array with said sample, mapping a grid (matrices) onto said second data image to create a registered second data image and comparing first and second registered data image to determine the presence or absence of said target analyte (Column 18, line 59-Column 19, line 53; Column 27, lines 30-50; and Fig. 10).

Walt et al further teach the array is decoded using a computer (Column 16, lines 11-15) wherein the computer is used for data analysis (Column 22, lines 8-13) but they do not specifically teach their obtained images are stored in a computer readable memory. However,

data image storage, comparison and analysis for target analyte determination was well known in the art at the time the claimed invention was made as taught by Gingeras et al (Column 4, line 33-Column, 5, line 67; Column 21, line 59-Column 22, line 21; and Fig. 34). Gingeras et al provide the motivation for using their computer image storage i.e. allows one to build up a data base of hybridization patterns corresponding to different species thereby facilitating species (or polymorphism) detection (Column 10, lines 40-67).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the computer stored images and comparison as taught by Gingeras et al to the image analysis of Walt et al for the expected benefit of building a data base of species-specific hybridization patterns thereby facilitating species detection as taught by Gingeras (Column 10, lines 40-67).

Regarding Claim 2, Walt et al disclose the method wherein said discrete sites are wells (Column 6, lines 22-29).

Regarding Claim 3, Walt et al disclose the method wherein said bioactive agents are proteins (Column 8, lines 50-59).

Regarding Claim 4, Walt et al disclose the method wherein said bioactive agents are nucleic acids (Column 9, lines 41-50).

Response to Arguments

11. Applicant argues that Walt et al does not teach the claimed method as newly claimed. The argument has been considered but is deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection discussed above.

12. Claims 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (U.S. Patent No. 6,327,410 B1, filed 11 September 1998) in view of Lockhart et al (U.S. Patent No. 6,040,138, filed 15 September 1995).

Regarding Claims 6-10, Walt et al disclose a signal preprocessing comprising acquiring a first data image (i.e. optical signature) of a random array composition comprising a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation each comprising a bioactive agent wherein said microspheres are distributed on said surface such that each of said discrete sites contain microspheres (Column 3, lines 35-45; Column 5, line 61-Column 6, line 29; and Fig. 5 & 7) determining the similarity of a first signal from at least one discrete site to at least one reference signal wherein when said first signal is similar to at least on of said reference signals, said discrete site contains a bead (Column 19, lines 31-53).

Walt et al further teach the discrete sites are ends of optical fibers whereby signals are detected through the optical fiber i.e. channel (Column 16, lines 21-65 and Fig. 4) wherein a signal from a first microsphere is measured through a first fiber and a signal from a second microsphere is measured through a second fiber (Column 16, lines 58-65).

Walt et al compare a first signal and second signal to determine bead presence (Column 19, lines 46-53) which clearly suggests that they compare the signal to a threshold signal (e.g. first signal) to determine presence of the bead. Additionally, signal detection and comparison to a threshold measure was well known in the art at the time the claimed invention was made as taught by Lockhart et al who teach a similar method of signal processing. The method of Lockhart et al comprises acquiring a first data image of the array (i.e. signal intensities of the control sample on the array) wherein the array comprises a substrate with a surface comprising discrete sites bioactive agent and obtaining a first signal from a discrete site and comparing the signal to a threshold measure (threshold intensity value) to thereby determine the presence of a bioactive agent at the site (Column 23, line 41-Column 24, line 6) whereby a

true signal is distinguished from a background signal. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the threshold measure of Lockhart et al to the signal detection and comparison of Walt et al to thereby determine presence or absence of a bead, to discard a signal below the threshold and to accurately analyze and distinguish signals from background signals as taught by Lockhart et al (Column 23, line 41-Column 24, line 6).

Response to Arguments

13. Applicant asserts that in contrast to Walt and Lockhart, the claimed invention compares a signal from a given bead with a threshold to determine if that bead falls within the spectrum of "true signal" but if the signal falls outside the threshold, the signal is not considered as true thereby allowing determination of bead. The argument has been considered but is not found persuasive because the claims are drawn to determining whether the site contains a bead, not determination of the bead or "true signal" or determining the presence of a bead of interest as asserted. Hence, the arguments are not commensurate in scope with the claims.

Applicant argues that the cited references do not provide a required motivation for their combination. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, a clear motivation has been provided as discussed above i.e. comparison of signal to a threshold provides accurate analysis and distinguishes signals from background signals as taught by Lockhart et al (Column 23, line 41-Column 24, line 6).

14. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al (U.S. Patent No. 6,040,138, filed 15 September 1995) in view of Walt et al (U.S. Patent No. 6,327,410 B1, filed 11 September 1998).

Regarding Claim 11, Lockhart et al disclose a method comprising acquiring a reference signal from subpopulations at discrete sites on an array (Column 23, lines 47-56) determining a threshold measure by comparing the reference signal to a threshold for each subpopulation (Column 23, line 57-Column 24, line 6) acquiring a first signal for each of a plurality of discrete sites and determining if the signal is within a threshold measure for the respective subpopulation (Column 23, line 42-Column 24, line 64). Lockhart et al do no specifically teach a subpopulation of microspheres. However, microsphere subpopulations were well known in the art at the time the claimed invention was made as taught by Walt et al who teach the bead-fiber array provides for very high density arrays of individually detectable beads (Column 4, line 59-Column 5, line 31). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the support of Lockhart with the bead-fiber substrate of Walt et al for the expected benefit of providing very high arrays of individually detectable beads as taught by Walt et al (Column 4, line 59-Column 5, line 31).

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 49, 53 and 54 of copending Application No. 09/636,387 in view of Walt et al (U.S. Patent No. 6,327,410). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of determining the presence of a target analyte comprising acquiring a data image and differ only in the instant claims are drawn to mapping a grid onto the data image to create a registered data image. However, grid mapping (i.e. matrices) to provide a registered data image (optical signature) was well known in the art at the time the claimed invention was made as taught by Walt et al who teach that matrices-forming optical signatures facilitate comparison of optical signature and analyte detection (Column 19, lines 31-52). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the'387 method by mapping a grid onto the data image to create the registered data image for the expected benefit of facilitating analyte detection as suggested by Walt et al (Column 19, lines 47-53).

17. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Comments

18. Applicant's intention to file a Terminal Disclaimer upon indication of allowable subject matter is acknowledged.

Conclusion

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

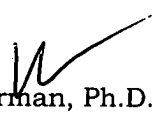
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



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Art Unit: 1634
July 8, 2004